REMARKS

I. Disposition of Claims

The restriction requirement of record has been made final. The elected embodiments include the following:

- medical device – stent
- matrix – fullerene
- antibody attachment – covalent
- vessel type – artery
- matrix attachment – covalent.

As of the mail date of the Office Action, claims 1-55 were pending. Upon entry of this Amendment, this disposition of claims is as follows:

- withdrawn – 6, 10-17, 19, 26, 33-37, 40, 42, 46, 48 and 51-55
- rejected/objected – 1-5, 7-9, 18, 20-25, 27, 29-32, 38, 39, 41, 43-45, 47, 49 and 50
  - allowable subject matter – claims 2, 28 and 44
  - canceled -- 43, 44, 47 , 49 and 50
  - new - 56-61

The Examiner's attention is directed to a possible inconsistency regarding the indication of allowable subject matter in Paragraphs 21 and 22 on page 12 of the Office Action. Specifically, the Examiner indicates that claims 2, 28 and 44 represent allowable subject matter. The undersigned Attorney respectfully submits that the Examiner may have committed an inadvertent error in the inclusion of claim 2 since that claim is rejected for prior art reasons under 35 U.S.C. §103. Instead of claim 2, the Examiner may have intended to indicate that claim 3 represented allowable subject matter.

Upon entry of this Amendment, the following claims read on the elected embodiments are eligible for examination on the merits: 1-5, 7-9, 18, 20-25, 27, 29-32, 38, 39, 41, 45 and 56-61.

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II. Amendments to the Specification and Claims

The original Abstract is alleged to contain legal phraseology, e.g., "This invention provides". Accordingly, the specification is objected to. The Abstract has been amended by the removal of any seemingly legal phraseology. A substitute page containing the amended Abstract is attached hereto and made a part of this Amendment. Removal of the objection to the specification is requested.

Claims 2, 3, 27, 43 and 44 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Claims 2 and 27 have been amended and there is now antecedent basis for the expression "the at least one layer of the matrix" as it appears in amended claims 2 and 27. Claims 43 and 44 have been canceled. Withdrawal of the §112 rejection is requested.

Independent claims 1, 18, 25, 29 and 38 have been amended to recite that the antibody reacts with an endothelial cell surface antigen. Support is found in the paragraph bridging pages 7-8 of the specification.

Claim 41 has been re-written to include the embodiment of claims 43 and 44, now cancelled. The Examiner indicated that claim 44 would be allowable if re-written to overcome the §112 rejection and to include the limitations of the base claim and any intervening claim.

New claims 56-61 are directed to a composition coating a medical device. Thus, these claims render moot the "intended use" of the composition. Support for these claims is provided by the specification, as originally filed. Furthermore, each of new claims 56-61 is readable on the elected embodiments.

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Applicants submit that no new matter has been introduced by any the amendments to the specification and/or claims.

III. Information Disclosure Statement and Oath/Declaration

Applicants are appreciative of the Examiner's indication that certain publications listed in the previously filed Information Disclosure Statements were not considered for failure to comply with 37 C.F.R. §1.98(a)(2). The publications are the three documents identified in Paragraph 5 at pages 3-4 of the Office Action. Applicants will submit a supplemental Information Disclosure Statement in due course to remedy the situation.

Applicants are mindful of the requirement to submit a new declaration as discussed in Paragraph 6 at page 4 of the Office Action. A new declaration will be submitted in due course.

IV. Claim Rejections – US 5,688,486 to Watson et al.

Claim 41, 45, 47 and 50 are rejected under 35 U.S.C. §102(b) as being anticipated by US 5,688,486 to Watson et al. ("Watson"). Claims 43 and 49 are rejected under 35 U.S.C. §103(a) as being unpatentable over Watson in view of US 5,338,571 to Mirkin et al. ("Mirkin").

Claim 41 has been re-written to include the embodiment of claims 43 and 44, now cancelled. The Examiner indicated that claim 44 would be allowable if re-written to overcome the §112 rejection and to include the limitations of the base claim and any intervening claim. In addition to claims 43, and 44, claims 47, 49 and 50 are cancelled.

Accordingly, the §102(b) rejection based on Watson and the §103(a) rejection based on the combination of Watson and Mirkin are moot. Withdrawal of the rejections is requested.

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V. Claim Rejections – Dekker et al.

In this Section V, Applicants will discuss the obviousness rejections under 35 U.S.C. §103(a) of medical device claims 1, 2, 4, 5, 7-9, 38 and 39 and method of treatment claims 29-32 (¶¶15-17 and 20 of the Office Action). The §103 rejection of each of these claims is based on the same combination of primary and secondary references. In certain instances, a tertiary reference is cited. Nevertheless, it would seem expedient for both the Examiner and Applicants to simultaneously address the §103 rejections of the medical device and method of treatment claims.

The primary reference is Dekker A. et al, *Thrombosis and Haemostasis*, "Improved Adhesion and Proliferation of Human Endothelial Cells on Polyethylene Precoated with Monoclonal Antibodies Directed against Cell Membrane Antigens and Extracellular Matrix Proteins", F.K. Schattauer Verlagsgesellschaft mbH (Stuttgart) 66(6) 715-724 (1991) ("Dekker"). The secondary reference is US 5,310,669 to Richmond et al. ("Richmond").

Dekker is directed to a specific study with a specific intent, purpose and function. As stated in the Introduction of Dekker:

> **...The present study deals with the effect of surface-adsorbed intact monoclonal antibodies on the adhesion and proliferation of human endothelial cells...Polyethylene was chosen as *model substrate*, since adhesion of endothelial cells onto the uncoated surface is low.** (Emphasis added)

Clearly, the express intent, purpose and function of the Dekker study requires the use of a "matrix-free" polyethylene graft as the model substrate. It was known that polyethylene would not interfere with the investigation of the effect of surface-adsorbed monoclonal antibodies directed against endothelial cell membrane proteins on the adhesion and proliferation of cultured

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human endothelial cells. Thus, the use of a "matrix-free" polyethylene surface must be considered a control of the Dekker investigation.

The Federal Circuit, and its predecessor, have consistently held that when an obviousness rejection is based on a modification that destroys the intent, purpose or function of the invention disclosed in the reference, such a proposed modification is not proper and the *prima facie* case of obviousness can not properly be made. Applicants rely on M.P.E.P. §2143.01 and the cases cited therein.

In Paragraph 15 of the Office Action at page 7, the Examiner correctly observes that Dekker "is silent to the medical device being coated with at least one layer of a matrix comprising fullerene ranging from about C60 to about C100". For this purpose, The Examiner relies on the secondary reference to Richmond. The Examiner alleges that Richmond discloses a substrate coated with a matrix comprising fullerene C60 with an antibody bound thereto. The Examiner concludes that it would have been obvious at the time claimed invention was made to modify Dekker by including a fullerene layer to the polyethylene graft precoated with monoclonal antibodies.

Applicants respectfully submit that the combination of Dekker and Richmond is improper since the modification of Dekker, as suggested by the Examiner, would render Dekker unsatisfactory for its intended purpose. As previously stated, the use of a "matrix-free" polyethylene surface must be considered a control of the Dekker investigation. Dekker purposefully chose a "matrix-free" polyethylene surface because of the known low adhesion of endothelial cells to the uncoated surface. Accordingly, in the absence of impermissible hindsight, there is no suggestion or motivation to add a fullerene coating to the "model substrate" chosen by Dekker.

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For all of the foregoing reasons, Applicants submit that a *prima facie* case of obviousness based on the combination of Dekker and Richmond has not been established with respect to medical device claims 1, 2, 4, 5, 7-9, 38 and 39 and method of treatment claims 29-32 (¶¶15-17 and 20 of the Office Action). The tertiary references to Watson, Asahara et al., Science 275: 964-967 (1997) ("Asahara") and Bos et al., Archives Phsio. Biochem 106; 100115 (1998) ("Bos") do not overcome the failure of Dekker and Richmond to suggest the claimed invention.

Withdrawal of the §103 rejection of medical device claims 1, 2, 4, 5, 7-9, 38 and 39 and method of treatment claims 29-32 is requested.

VI. Claim Rejections – Richmond

This Section discusses the obviousness rejection under 35 U.S.C. §103(a) of composition claims 18, 20-25 and 27 (¶¶18 and 19 of the Office Action). These claims are directed to a composition for coating a medical device with a composition comprising a matrix and a therapeutically effective amount of at least one type of antibody that reacts with an endothelial cell surface antigen. With respect to the §103 rejection of the composition claims, the Examiner again relies on the Dekker and Richmond. However, in this case, the primary reference is Richmond and the secondary reference is Dekker.

Richmond discloses fullerene-coated cell culture surfaces, e.g., flasks, cell culture dishes, cell culture microcarriers, cell culture macrocarriers, cell culture films and cell culture fibers (col. 3, lines 43-47). Richmond does not disclose or suggest the use of an actual medical device such as a stent or graft. At the bottom of page 9 of the Office Action, the Examiner states that "[i]t would have been obvious...at the time of applicant's invention to look to the teachings of Dekker et al. to make the substrate of Richmond et al. a medical device..."

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As discussed in Section V, above, Dekker discloses a "matrix-free" polyethylene graft precoated with monoclonal antibodies. The use of this "model substrate" by Dekker is key to the investigation of the effect of surface-adsorbed monoclonal antibodies directed against endothelial cell membrane proteins on the adhesion and proliferation of cultured human endothelial cells. Therefore, contrary to the Examiner's statement at the bottom of page 9 of the Office Action, it would not have been obvious to look to Dekker to substitute the fullerene-coated cell culture surface of Richmond with a medical device. In view of the express teachings of Dekker, there is no suggestion to make such a substitution.

Furthermore, Richmond provides a general disclosure of antibodies bound to a fullerene-coated surface. No working example is given wherein antibodies are attached to a fullerene-coated surface. In contrast to Richmond, Dekker discloses a specific class of monoclonal antibodies that are precoated directly onto the surface of a polyethylene graft. As previously discussed, it is contrary to the intent, function and purpose of Dekker to precoat such antibodies on a surface other than the model polyethylene surface.

For all of the foregoing reasons, Applicants submit that a *prima facie* case of obviousness based on the combination of Richmond and Dekker has not been established with respect to composition claims 18, 20-25 and 27 (¶¶18 and 19 of the Office Action). The tertiary reference to Asahara does not overcome the failure of Richmond and Dekker to suggest the invention of claim 23.

Withdrawal of the §103 rejection of composition claims 18, 20-25 and 27 is requested.

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CONCLUSION

Applicants have made a good faith attempt to respond to the Office Action. Claims 1-5, 7-9, 18, 20-25, 27, 29-32, 38, 39, 41, 45 and 56-61 are directed to patentable subject matter. Accordingly, Applicants request reconsideration and allowance of the claims.

Any additional fee due in connection with this communication should be charged to Deposit Account No. 23-1703.

Dated: January 16, 2004

Respectfully submitted,

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Attachment: Abstract

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